PLAINTIFF

Miscellaneous

ORIGINAL

EXHIBIT

3

1 Through 14

3 EXHIBIT 1

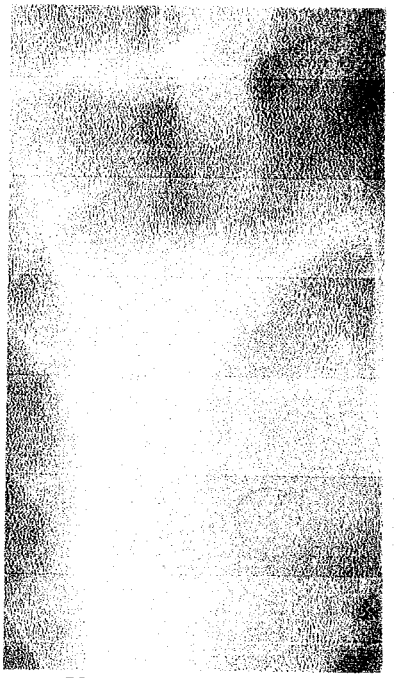
Paget's disease of bone

From Wikipedia, the free encyclopedia

Paget's disease, otherwise known as **osteitis deformans**, is a chronic disorder that typically results in enlarged and deformed bones. It is named after Sir James Paget, the British surgeon who first described this disease[1]. The excessive breakdown and formation of bone tissue that occurs with Paget's disease can cause bone to weaken, resulting in bone pain, arthritis, deformities, and fractures. Paget's disease may be caused by a slow virus infection (i.e., paramyxoviruses such as measles and respiratory syncytial virus), present for many years before symptoms appear. There is also a hereditary factor since the disease may appear in more than one family member.

Paget's disease is rarely diagnosed in people less than 40 years of age. Men are more commonly affected than women. Prevalence of Paget's disease ranges from 1.5 to 8 percent depending on age and country of residence. Prevalence of familial Paget's disease (where more than one family member has the disease) ranges from 10 to 40 percent in different parts of the world.Because early diagnosis and treatment is important, after age 40, siblings and children of someone with Paget's disease may wish to have an alkaline phosphatase blood test every 2 or 3 years. If the alkaline phosphatase level is above normal, other tests such as a bone-specific alkaline phosphatase test, bone scan, or x-ray can be performed.

Paget's disease of bone
Classification & external resources



X-ray of Paget's disease

ICD-10	M88.
ICD-9	731.0
OMIM	602080
DiseasesDB	9479
MedlinePlus	000414
eMedicine	med/2998 radio/514 pmr/98
MeSH	D010001

Contents

Symptoms

Many patients do not know they have Paget's disease because they have a mild case with no symptoms. Sometimes, symptoms may be confused with those of arthritis or other disorders. In other cases, the diagnosis is made only after complications have developed. Symptoms can include:

- Bone pain is the most common symptom. Bone pain can occur in any bone affected by Paget's disease. It often localizes to areas adjacent to the joints.
- Headaches and hearing loss may occur when Paget's disease affects the skull.
- Pressure on nerves may occur when Paget's disease affects the skull or spine.
- Somnolence (drowsiness) due to vascular steal syndrome of the skull.
- Paralysis due to vascular steal syndrome of the vertebrae.
- Increased head size, bowing of limb, or curvature of spine may occur in advanced cases.
- Hip pain may occur when Paget's disease affects the pelvis or thighbone.
- Damage to joint cartilage may lead to arthritis.
- Teeth may spread intraorally.
- Chalkstick fractures.

Diagnosis

Paget's disease may be diagnosed using one or more of the following tests:

- Pagetic bone has a characteristic appearance on x-rays. A skeletal survey is therefore indicated.
- An elevated level of alkaline phosphatase in the blood in combination with normal calcium, phosphate, and aminotransferase levels in an elderly patient are suggestive of Paget's disease.
- Bone scans are useful in determining the extent and activity of the condition. If a bone scan suggests Paget's disease, the affected bone(s) should be x-rayed to confirm the diagnosis.

Prognosis

The outlook is generally good, particularly if treatment is given before major changes in the affected bones have occurred. Any bone or bones can be affected, but Paget's disease occurs most frequently in the spine, skull, pelvis, thighs, and lower legs. In general, symptoms progress slowly, and the disease does not spread to normal bones. Treatment can control Paget's disease and lessen symptoms but is not a cure. Osteogenic sarcoma, a form of bone cancer, is an extremely rare complication that occurs in less than one percent of all patients.

Other medical conditions

Paget's disease may lead to other medical conditions, including:

- Arthritis: Long bones in the leg may bow, distorting alignment and increasing pressure on nearby joints. In addition, Pagetic bone may enlarge, causing joint surfaces to undergo excessive wear and tear. In these cases, pain may be due to a combination of Paget's disease and osteoarthritis.
- Loss of hearing in one or both ears may occur when Paget's disease affects the skull and the bone that surrounds the inner ear. Treating the Paget's disease may slow or stop hearing loss. Hearing aids may also help. It is believed by some that the disease was responsible for Beethoven's deafness.
- Cardiovascular disease: In severe Paget's disease (i.e. with more than 15% skeletal involvement), the heart works harder to pump blood to affected bones. Left ventricular hypertrophy is an associated finding. High-output congestive failure may rarely occur. Similarly, calcification of the aortic valve and associated vessels may occur due to turbulent flow caused by increased cardiac output.
- Kidney stones are somewhat more common in patients with Paget's disease.

- Nervous system: Pagetic bone can cause pressure on the brain, spinal cord, or nerves, and reduced blood flow to the brain and spinal cord.
- Sarcoma: Rarely, Paget's disease is associated with the development of a malignant tumor of bone. When there is a sudden onset or worsening of pain, sarcoma should be considered.
- When Paget's disease affects the facial bones, the teeth may become loose. Disturbance in chewing may occur.
- Rarely, when the skull is involved, the nerves to the eye may be affected, causing some loss of vision.

Paget's disease is not associated with osteoporosis. Although Paget's disease and osteoporosis can occur in the same patient, they are different disorders. Despite their marked differences, several treatments for Paget's disease are also used to treat osteoporosis.

Treatment

Types of physicians

The following types of medical specialists are generally knowledgeable about treating Paget's disease.

- Endocrinologists -- Internists who specialize in hormonal and metabolic disorders.
- Rheumatologists -- Internists who specialize in joint and muscle disorders.
- Specialists -- Orthopedic surgeons, neurologists, and otolaryngologists (physicians who specialize in ear, nose, and throat disorders) may be called upon to evaluate specialized symptoms.

Drug therapy

The goal of treatment is to relieve bone pain and prevent the progression of the disease. The U.S. Food and Drug Administration has approved the following treatments for Paget's disease:

Bisphosphonates

Five bisphosphonates are currently available. In general, the most commonly prescribed are the three most potent bisphosphonates: Actonel®, Fosamax® and Aredia®. Didronel® and Skelid® may be appropriate therapies for selected patients but are less commonly used. As a rule, bisphosphonate tablets should be taken with 6-8 oz of tap water on an empty stomach. None of these drugs should be used by people with severe kidney disease.

- Didronel® (etidronate disodium) -- Tablet; approved regimen is 200-400 mg once daily for 6 months; the higher dose (400 mg) is more commonly used; no food, beverages, or medications for 2 hours before and after taking; course should not exceed 6 months, but repeat courses can be given after rest periods, preferably of 3-6 months duration.
- Aredia® (pamidronate disodium) -- Intravenous; approved regimen 30 mg infusion over 4 hours on 3 consecutive days; more commonly used regimen 60 mg over 2-4 hours for 2 or more consecutive or non-consecutive days.
- Fosamax® (alendronate sodium) -- Tablet; 40 mg once daily for 6 months; patients should wait at least 30 minutes after taking before eating any food, drinking anything other than tap water, taking any medication, or lying down (patient may sit).
- Skelid® (tiludronate disodium) -- Tablet; 400 mg (two 200 mg tablets) once daily for 3 months; may be taken any time of day, as long as there is a period of 2 hours before and after resuming

food, beverages, and medications.
- Actonel® (risedronate sodium) -- Tablet; 30 mg once daily for 2 months; patients should wait at least 30 minutes after taking before eating any food, drinking anything other than tap water, taking any medication, or lying down (patient may sit).

Calcitonin

- Miacalcin® is administered by injection; 50 to 100 units daily or 3 times per week for 6-18 months. Repeat courses can be given after brief rest periods. Miacalcin may be appropriate for certain patients but is seldom used. The nasal spray form of this drug is not approved for the treatment of Paget's disease.

Surgery

Medical therapy prior to surgery helps to decrease bleeding and other complications. Patients who are having surgery should discuss pre-treatment with their physician. There are generally three major complications of Paget's disease for which surgery may be recommended.

- Fractures -- Surgery may allow fractures to heal in better position.
- Severe degenerative arthritis -- If disability is severe and medication and physical therapy are no longer helpful, joint replacement of the hips and knees may be considered.
- Bone deformity -- Cutting and realignment of Pagetic bone (osteotomy) may help painful weight-bearing joints, especially the knees.

Complications resulting from enlargement of the skull or spine may injure the nervous system. However, most neurologic symptoms, even those that are moderately severe, can be treated with medication and do not require neurosurgery.

Diet and Exercise

In general, patients with Paget's disease should receive 1000-1500 mg of calcium, adequate sunshine, and at least 400 units of vitamin D daily. This is especially important in patients being treated with bisphosphonates. Patients with a history of kidney stones should discuss calcium and vitamin D intake with their physician.

Exercise is very important in maintaining skeletal health, avoiding weight gain, and maintaining joint mobility. Since undue stress on affected bones should be avoided, patients should discuss any exercise program with their physician before beginning.

References

1. ^ Paget J., *On a form of chronic inflammation of bones (osteitis deformans)*, Trans Med-Chir Soc, 1877,60,37:63

Retrieved from "http://en.wikipedia.org/wiki/Paget%27s_disease_of_bone"

Categories: All articles with unsourced statements | Articles with unsourced statements since February 2007 | Skeletal disorders

EXHIBIT 2

MayoClinic.com
Tools for healthier lives

Received by t on Feb 6, 2008

Original Article:http://www.mayoclinic.com/health/pagets-disease-of-bone/DS00485

Paget's disease of bone

Introduction

Paget's disease of bone is a condition that affects the normal biological processes of your bones. The disease is named after a mid-19th-century English surgeon, Sir James Paget, who also identified Paget's disease of the breast. Other than sharing his name, however, the two conditions are unrelated.

Even after you've reached your full height, your bones don't stop growing. Bone is living tissue engaged in a continual process of renewal. During this constant process called remodeling, old bone is removed and replaced by new bone. Paget's disease of bone disrupts this process. Early in the course of the disease, old bone starts breaking down faster than new bone can be built. Over time, your body responds by generating new bone at a faster than normal rate. This rapid remodeling produces bone that's softer and weaker than normal bone, which can lead to bone pain, deformities and fractures.

Paget's disease of bone becomes more common with age. It usually affects the skull, the spine and the bones in your arms, legs and pelvis. The disease may affect only one or two areas of your body, or may be widespread.

Often, people with Paget's disease of bone have no symptoms at all and may not require treatment other than regular monitoring. But if signs or symptoms are troublesome, treatment for Paget's disease of bone is available in the form of medications or surgery.

Signs and symptoms

Paget's disease of bone affects each person differently. Most people with Paget's disease have no symptoms. When symptoms do occur, they typically present in specific areas affected by the disease, although they may be widespread. Affected areas may include:

- **Bones.** Pain in the affected bones is the most common symptom of

Paget's disease of bone. Your pain may be constant, aching and deep, and may be most severe at night.

- **Joints.** Paget's disease may damage the cartilage lining the joints near your affected bones. This wear and tear often leads to osteoarthritis in your affected joints, a condition that may cause pain, swelling and stiffness.
- **Nerves.** Enlarged bones can compress your spinal cord or the nerves exiting your brain and spinal cord. Pain resulting from nerve compression is more severe than the bone pain associated with Paget's. The location of the pain caused by nerve compression depends on the nerve that's affected. You may notice pain radiating from your lower back into your legs (sciatica) if the lower region of your spine is affected. Pressure on a nerve can also cause numbness, tingling, weakness, hearing loss and double vision.

Other signs and symptoms of Paget's disease may include:

- Warmth in your skin over the affected area
- Neurological problems, such as hearing loss, headache and rarely, vision loss
- Bone deformities, such as bowlegs and enlarged head size
- Fractures

Causes

Scientists haven't identified a cause of Paget's disease of bone, though they have discovered several genes that appear to be linked to the disorder.

Some scientists believe Paget's is related to a viral infection in your bone cells that may be present for many years before problems appear. Hereditary factors seem to influence whether you're susceptible to the disease.

Risk factors

Age and heredity are the only known risk factors for Paget's disease of bone. Occasionally, the disease runs in families. People older than 40 are the most likely to develop Paget's disease. Men are more commonly affected than women.

When to seek medical advice

Talk to your doctor if you have:

- Symptoms of Paget's disease of bone, such as pain in your bones

and joints
- Symptoms of pinched nerves, such as pain, tingling and weakness
- Bone deformities

If you have Paget's disease of bone, contact your doctor if you experience:

- Signs and symptoms of the disease affecting your skull, such as hearing or vision loss, double vision, facial weakness or numbness
- Loss of bladder or bowel control accompanied by weakness in your legs, which can indicate severe spinal damage
- Sudden or severe pain or a change in the pain that you've been experiencing

Screening and diagnosis

CLICK TO ENLARGE


Paget's disease of bone

Detecting Paget's disease of bone early may help prevent serious complications. The following procedures may help your doctor detect Paget's disease of bone:

- **Blood test.** If you have a sibling or parent with Paget's disease, talk to your doctor about requesting an alkaline phosphatase blood test every two to three years after age 40. Alkaline phosphatase is produced by bone cells that are responsible for forming new bone and is elevated in most people with Paget's disease.
- **X-rays.** The first indication of Paget's disease is often either an elevated alkaline phosphatase level or abnormalities found on X-rays done for other reasons. X-ray images of your bones can show areas of bone reabsorption, enlargement of the bone and deformities that are characteristic of Paget's disease, such as bowing of your long bones. Your doctor may be able to base a diagnosis of Paget's disease on the bone X-ray findings.
- **Bone scan.** In some cases, your doctor may recommend a bone scan. Bone scans can pick up Paget's disease before it can be seen on an X-ray. Doctors also use bone scans to determine which bones are affected. In a bone scan, radioactive tracers are injected into your body. The tracers are taken up by your bones and give off radiation that is captured by a special camera, which produces a

picture of your skeleton. Areas of bone that are affected by Paget's disease are darker than normal on the scan.

Complications

In most cases, Paget's disease of bone progresses slowly. The disease can be managed effectively in nearly all people and is rarely fatal. Possible complications include:

- **Osteoarthritis.** This degenerative joint disease is a common long-term complication of Paget's disease.
- **Heart failure.** Unusually extensive Paget's disease may force your heart to work harder to pump blood to the affected areas of your body. In people with pre-existing heart disease, this increased workload can lead to heart failure.
- **Sarcoma.** A rare complication is a bone cancer known as sarcoma, also called osteosarcoma or osteogenic sarcoma, which may develop in bones affected by Paget's disease. This complication occurs in less than 1 percent of people with Paget's disease and usually doesn't develop until many years after the onset of Paget's.

If the disease affects bones in your head, you may experience hearing loss, loss of teeth and, rarely, loss of vision.

Treatment

If you don't have symptoms, you may not need treatment. However, if the disease is active — indicated by an elevated alkaline phosphatase level — and is affecting high-risk sites in your body, such as your skull or spine, your doctor may recommend treatment to prevent complications, whether or not you have symptoms.

Treatment for Paget's disease can help alleviate pain and may halt the damage done to your bones. In many cases, treatment can cause remission of the disease, which may be prolonged in some people.

Doctors generally recommend treatment when:

- You experience bone pain or neurological signs or symptoms related to Paget's disease.
- You're planning to have surgery to repair damage related to Paget's disease. In this case, your doctor will prescribe medications to minimize blood loss during the operation.
- You're at risk of serious, long-term complications due to the aggressiveness of your disease and the location of your affected

bones. Involvement of the spine, skull, bones near major joints, and the long bones of the arms and legs is more likely to result in complications.

- Your heart is overworked because of widespread Paget's disease.

If any of the above criteria apply to you, your doctor may recommend treatment.

Medications

Your doctor may recommend bone-regulating medications if you have Paget's-related pain or if you're at risk of serious complications. Doctors use two kinds of medications to treat Paget's disease of bone:

- **Bisphosphonates.** Doctors commonly use these medications to treat osteoporosis and increase bone density, but they may also use them to reduce the activity of Paget's disease. Treatment with these agents helps restore more-normal-appearing bone and may produce long-term remission of Paget's disease. Bisphosphonates are currently the treatment of choice for Paget's disease, but you can't take them if you have serious kidney disease.

  Oral bisphosphonates are generally well tolerated, but may irritate your gastrointestinal tract. Some bisphosphonates aren't available as oral medications, and you must receive them through a vein (intravenously). Intravenous administration offers a more rapid response than oral medications do and provides an option when you can't tolerate or are not a candidate for oral bisphosphonates.

  Doctors usually prescribe bisphosphonates for two to six months, depending on the drug used. You may need to switch to another brand if you take these medications long term because resistance to one bisphosphonate may build over time.

- **Calcitonin.** If you can't tolerate bisphosphonates, your doctor may prescribe calcitonin (Miacalcin), a naturally occurring hormone involved in calcium regulation and bone metabolism. Calcitonin is a drug that you administer to yourself by injection.

  Side effects may include nausea, facial flushing and irritation at the injection site. Stopping treatment with calcitonin usually results in a rapid reactivation of the disease and recurrence of symptoms.

Your doctor may use blood tests measuring your alkaline phosphatase level to monitor your response to these medications. If therapy is effective, your alkaline phosphatase level will decrease and may return to normal.

Dealing with arthritis

Paget's disease may also require treatment to reduce pain or treat the inflammation associated with arthritis. Treatment options include:

- **Nonsteroidal anti-inflammatory drugs (NSAIDs).** NSAIDs alleviate pain and reduce the inflammation that's often the source of pain in arthritis related to Paget's disease. NSAIDs come in prescription and nonprescription forms. You may need to try more than one NSAID before finding the one that's most effective for you. Long-term use of NSAIDs or use of more than one NSAID can cause side effects, such as ulcers, heartburn, nausea and stomach bleeding. Large doses of NSAIDs can lead to kidney problems.
- **Acetaminophen.** Acetaminophen (Tylenol, others) may provide some relief of your pain, but it doesn't improve inflammation. It's generally safe if you take it for a short period of time and adhere to the daily dosage guidelines. If taken at the maximum dose for extended periods of time — especially when combined with regular alcohol intake — acetaminophen may damage your liver.

Surgery

In rare cases, you may require surgery to help fractures heal, to replace joints damaged by severe arthritis or to realign deformed bones. If Paget's disease affects your spine or your skull, you may need surgery to reduce pressure on nerves and prevent serious complications.

Paget's disease often causes the body to produce an excessive number of blood vessels (hypervascularity) in the affected bones. This change increases the risk of serious blood loss during an operation. If you're scheduled for surgery that involves bones affected by Paget's disease, your doctor may prescribe medications to reduce the activity of the disease, a step that tends to reduce blood loss during surgery.

Self-care

Take the following steps to reduce your risk of complications from Paget's disease of bone:

- **Prevent falls.** Paget's disease puts you at high risk of bone fractures. Ask your doctor for advice on preventing falls. He or she may recommend that you use a cane or a walker. Take measures to fall-proof your home. Remove slippery floor coverings, use nonskid mats in your bathtub or shower, tuck away cords, and install handrails on stairways and grab bars in your bathroom.
- **Eat well.** Be sure your diet includes adequate levels of calcium and of vitamin D, which facilitates the absorption of calcium. This is especially important if you're being treated with bisphosphonates. Generally, you need at least 1,000 milligrams (mg) a day of calcium and 400 international units (IU) or 10 micrograms (mcg) a day of

vitamin D. Review your diet with your doctor and ask him or her whether you should begin taking vitamin and calcium supplements.

- **Exercise regularly**. Exercising on a regular basis is essential for maintaining joint mobility and bone strength. Focus on weight-bearing exercise — such as walking, jogging or dancing — to maximize the benefit to your bones. Be sure to include strength training in your exercise program — strong muscles help support damaged joints. Talk to your doctor before beginning an exercise program to determine the right type, duration and intensity of exercise for you. Some activities may stress your affected bones.
- **Maintain a healthy weight.** Excess body weight may cause additional damage to your joints and may worsen pain in your joints. If you require surgery, excess weight also increases the risk of complications.

Coping skills

Living with a chronic condition such as Paget's disease of bone, even if you don't have symptoms, can be stressful. Focus on what you can do to reduce your risk of complications, such as exercising regularly and eating a healthy diet. Discuss any new symptoms or changes in your symptoms with your doctor. Effective treatments are available.

You may also find it helpful to join a support group for people with Paget's disease. To learn about support resources available in your area, contact The Paget Foundation.

By Mayo Clinic Staff
Aug 15, 2006

DS00485

EXHIBIT 3

close window

Source: http://www.medicinenet.com

Paget's Disease

Medical Author: William C. Shiel Jr., MD, FACP, FACR

What is Paget's disease?

Paget's disease is a chronic bone disorder that is due to irregular breakdown and formation of bone tissue. Paget's disease can cause bones to expand and weaken and may result in bone pain, arthritis, bone deformity and fractures. It is usually localized to one bone but can involve many bones. The actual cause of Paget's disease is not known. Paget's disease is also known as osteitis deformans.

Who gets Paget's disease?

Paget's disease is rarely diagnosed in people under 40 years of age. Men and women are approximately equally affected. The prevalence of Paget's disease ranges from 1.5%-8% depending on age and country of residence. The prevalence of familial Paget's disease (where more than one family member has the disease) ranges from 10%-40% in different parts of the world. Because early diagnosis and treatment is important, after age 40, brothers, sisters and children of someone with Paget's disease may wish to have an alkaline phosphatase

frequently in the spine, skull, pelvis, thighs, and lower legs. In general, symptoms progress slowly, and the disease does not spread to normal bones. Treatment can control Paget's disease and lessen symptoms, but it's not a cure.

What other medical problems can be caused by Paget's disease?

Paget's disease may lead to other medical conditions, including:

- **Arthritis**—Long bones in the leg may bow, distorting alignment and increasing pressure on nearby joints. In addition, Pagetic bone may enlarge, causing joint surfaces to undergo excessive wear and tear. In these cases, pain may be due to a combination of Paget's disease and osteoarthritis.
- **Hearing loss**—Loss of hearing in one or both ears may occur when Paget's disease affects the skull and the bone that surrounds the inner ear. Treating the Paget's disease may slow or stop hearing loss. Hearing aids may also help.
- **Heart disease**—In severe Paget's disease, the heart works harder to pump blood to affected bones. This usually does not result in heart failure except in some people who also have hardening of the arteries.
- **Kidney stones**—Kidney stones are somewhat more common in patients with Paget's disease.
- **Nervous system pressure**—Pagetic bone can cause pressure on the brain, spinal cord, or nerves, and reduced blood flow to the brain and spinal cord.
- **Bone sarcoma**—Paget's disease is associated with the development of osteosarcoma, a malignant tumor of bone. It is, fortunately, rare and occurs in less than 1% of all patients with Paget's disease. However, when there is a sudden onset or worsening of pain, sarcoma should be considered.
- **Teeth loosening**—When Paget's disease affects the facial bones, the teeth may become loose. Disturbance in chewing may also occur.
- **Decreased vision**—Rarely, when the skull is involved, the nerves to the eye may be affected, causing some loss of vision.

What is the relationship between Paget's disease and osteoporosis?

None. Paget's disease is not associated specifically with osteoporosis. Although Paget's disease and osteoporosis can occur in one and the same person, they are completely different disorders. But despite their marked differences, many treatments for Paget's disease can also be used to treat osteoporosis.

What type of medical specialists are generally knowledgeable about

blood test every two or three years. If the alkaline phosphatase level is above normal, other tests such as a bone-specific alkaline phosphatase test, bone scan, or x-ray can be done.

What are the symptoms of Paget's disease?

Many people do not know they have Paget's disease because they have a mild case of the disease with no symptoms. Sometimes, symptoms may be confused with those of arthritis or other disorders. In other cases, the diagnosis is made only after complications have developed. Symptoms can include:

- **Bone pain** is the most common symptom. Bone pain can occur in any bone affected by Paget's disease and is often worse at night. It often localizes to areas adjacent to the joints and can be accompanied by warmth to the touch.
- **Headaches and hearing loss** may occur when Paget's disease affects the skull.
- **Pressure on nerves** may occur when Paget's disease affects the skull or spine.
- **Increased head size, bowing of limb, or curvature of spine** may occur in advanced cases.
- **Hip pain** may occur when Paget's disease affects the pelvis or thighbone.
- **Damage to cartilage of joints** may lead to arthritis.

How is the diagnosis made of Paget's disease?

Paget's disease may be diagnosed using one or more of the following tests:

- **X-rays**—Pagetic bone has a characteristic appearance on x-rays.
- **Alkaline phosphatase test**—An elevated level of alkaline phosphatase in the blood can be suggestive of Paget's disease but can be found in other conditions.
- **Bone scan**—This is useful in determining the extent and activity of the condition. If a bone scan suggests Paget's disease, the affected bone or bones should be x-rayed to confirm the diagnosis.

What is the prognosis (outlook) with Paget's disease?

The outlook is generally good, particularly if treatment is given before major changes in the affected bones have occurred. Paget's disease occurs most

treating Paget's disease?

The following types of medical specialists are, as a rule, generally knowledgeable about treating Paget's disease:

- Endocrinologists—internists who specialize in hormonal and metabolic disorders.
- Rheumatologists—internists who specialize in joint, muscle, and immune disorders.
- Other specialists—Orthopedic surgeons, neurologists, and otolaryngologists (physicians who specialize in ear, nose, and throat disorders) may be called upon to evaluate and treat certain symptoms.

What is the goal of drug treatment?

The goal of treatment is to control Paget's disease activity for as long a period of time as possible. Incidentally detected Paget's disease that is not associated with symptoms may require no treatment. Treatment options include aspirin, other anti-inflammatory medications, pain medications, and medications that slow the rate of bone turnover, such as calcitonin (Calcimar, Miacalcin), etidronate (Didronel), alendronate (Fosamax), and pamidronate (Aredia). A newer drug, risedronate (Actonel), appears to have a powerful effect against severe Paget's disease. It has the added advantage of requiring only two months of initial treatment and is given by mouth.

What medications are approved for Paget's disease?

The U.S. Food and Drug Administration (FDA) has approved the following treatments for Paget's disease:

Bisphosphonates

Five bisphosphonates are currently available for Paget's disease. As a rule, oral bisphosphonate tablets should be taken with 6-8 oz. of tap water on an empty stomach. None of these drugs should be used by people with severe kidney disease. If tolerable, bisphosphonates are the first option of treatment.

- Didronel (etidronate disodium)—tablet; approved regimen is 200-400 mg once daily for six months; the higher dose (400 mg) is more commonly used; no food, beverages, or medications for two hours before and after taking; course should not exceed six months, but repeat courses can be given after rest periods, preferably of three to six months duration
- Aredia (pamidronate disodium)—intravenous (particularly helpful for those patients who cannot tolerate oral bisphosphonates due to gastrointestinal

toxicity); approved regimen 30 mg infusion over four hours on three consecutive days; more commonly used regimen 60 mg over two to four hours for two or more consecutive or nonconsecutive days

- Fosamax (alendronate sodium)—tablet; 40 mg once daily for six months; patients should wait at least 30 minutes after taking before eating any food, drinking anything other than tap water, taking any medication, or lying down (patient may sit)
- Skelid (tiludronate disodium)—tablet; 400 mg (two 200 mg tablets) once daily for three months; may be taken any time of day, as long as there is a period of two hours before and after resuming food, beverages, and medications
- Actonel (risedronate sodium)—tablet; 30 mg once daily for two months; patients should wait at least 30 minutes after taking before eating any food, drinking anything other than tap water, taking any medication, or lying down (patient may sit)

Calcitonin

- Miacalcin is administered by injection; 50 to 100 units daily or three times per week for six to 18 months.

When may surgery be recommended for Paget's disease?

Medical therapy prior to surgery helps to decrease bleeding and other complications. Patients who are having surgery should discuss pretreatment with their physician. There are generally three major complications of Paget's disease for which surgery may be recommended.

- **Fractures**—Surgery may allow fractures to heal in better position.
- **Severe degenerative arthritis**—If disability is severe and medication and physical therapy are no longer helpful, joint replacement of the hips and knees may be considered.
- **Bone deformity**—Cutting and realignment of Pagetic bone (osteotomy) may help painful weight-bearing joints, especially the knees.

Complications resulting from enlargement of the skull or spine may injure the nervous system. However, most neurologic symptoms, even those that are moderately severe, can be treated with medication and do not require neurosurgery.

How do diet and exercise help in Paget's disease?

In general, people with Paget's disease should receive 1,000-1,500 mg of

calcium, adequate sunshine, and at least 400 units of vitamin D daily. This is especially important in patients being treated with bisphosphonates. Patients with a history of kidney stones should discuss calcium and vitamin D intake with their physician.

Exercise is very important in maintaining skeletal health, avoiding weight gain, and maintaining joint mobility. Since undue stress on affected bones should be avoided, patients should discuss any exercise program with their physician before beginning.

Who discovered Paget's disease?

Paget's disease is named after the English surgeon, Sir James Paget, who described it in 1877. Paget also discovered the worm that causes trichinosis and described what is called Paget's disease of the breast. Together with Rudolph Virkow in Germany, Paget was one of the founders of pathology.

Where can I find more information about Paget's disease?

For further information, you can contact:

The Paget's Disease Foundation
120 Wall Street
Suite 1602
New York, NY 10005-4001
212-509-5335
212-509-8492 Fax
email: pagetfdn@aol.com

Paget's Disease At A Glance

- Paget's disease is a chronic bone disorder.
- Paget's disease frequently causes no symptoms.
- Paget's disease can cause pain in the bones or joints, headaches and hearing loss, pressure on nerves, increased head size, bowing of limb, or curvature of spine.
- Tests used to diagnose Paget's disease include x-rays, blood tests, and bone scanning.
- Paget's disease can lead to other medical conditions.
- Treatment options include aspirin, other anti-inflammatory medications, pain medications, and medications that slow the rate of bone turnover.

Reference: Paget's Disease. *New England Journal of Medicine* 2006;355:593-600.

EXHIBIT 4

Diagnosing Paget's Disease of Bone

Many patients who have Paget's disease of bone do not know that they have it, since the disease may be so mild that it is not detected. Sometimes, the patient's doctor is alerted to the possibility of Paget's disease when a blood test reveals an elevated level of serum alkaline phosphatase (SAP). Sometimes the patient's symptoms are confused with arthritis or other disorders. In other cases, the diagnosis is made only after complications have developed.

Q. What is SAP?

A. SAP is a chemical (enzyme) that is produced by bone cells and is over-produced by Pagetic bone. SAP is measured by using a routine blood test. A SAP level that is higher than normal, provided that there is no evidence of liver disease, probably indicates that the source of elevated SAP is bone rather than some other part of the body. A mild increase in SAP level (up to twice the normal level) might indicate Paget's disease or another problem, such as a healing fracture. A SAP level two or more times higher than normal strongly suggests Paget's disease, especially if serum calcium and phosphorus, as well as renal (kidney) function, are normal.

The range of SAP that is considered normal varies considerably depending on the laboratory used for the test. A typical "normal" range for a person over the age of 60 may range from 20-120 units.

In addition to its use in diagnosis, measurement of SAP is an important tool for monitoring a patient's response to therapy for Paget's disease. In some patients it may be necessary to measure the *serum bone alkaline phosphatase*, using a special test which is helpful in assessing bone disease in patients with abnormal liver function. In some cases urinary markers of bone resorption such as N-telopeptide are also used to monitor the response the treatment.

Q. What is a bone scan and how is it used to diagnose Paget's disease?

A. A bone scan is another way to identify bones affected by Paget's disease. When a bone scan is performed, a safe amount of a radioactive substance is injected and circulates through the bloodstream, showing areas of the skeleton where Paget's disease might be present.

Q. How are X-rays used to diagnose Paget's disease?

A. X-rays are used alone or in conjunction with bone scans to confirm or eliminate the presence of Paget's disease. Bones affected by Paget's disease have a characteristic appearance on x-rays.

Q. When may a bone biopsy be used to diagnose Paget's disease?

A. Rarely, a bone biopsy may be required if the x-ray is not conclusive.

(Over)

Summary: Key factors for diagnosing Paget's disease are an elevated SAP and an x-ray showing pagetic bone.

For additional information, contact:

The Paget Foundation
120 Wall Street, Suite 1602
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Tel: (800) 23-Paget or (212) 509-5335
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Email: pagetfdn@aol.com
http://www.paget.org

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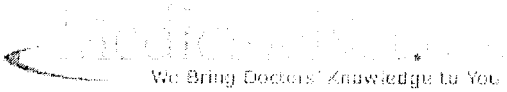

Source: http://www.medicinenet.com

Paget's Disease

Medical Author: William C. Shiel Jr., MD, FACP, FACR

What is Paget's disease?

Paget's disease is a chronic bone disorder that is due to irregular breakdown and formation of bone tissue. Paget's disease can cause bones to expand and weaken and may result in bone pain, arthritis, bone deformity and fractures. It is usually localized to one bone but can involve many bones. The actual cause of Paget's disease is not known. Paget's disease is also known as osteitis deformans.

Who gets Paget's disease?

Paget's disease is rarely diagnosed in people under 40 years of age. Men and women are approximately equally affected. The prevalence of Paget's disease ranges from 1.5%-8% depending on age and country of residence. The prevalence of familial Paget's disease (where more than one family member has the disease) ranges from 10%-40% in different parts of the world. Because early diagnosis and treatment is important, after age 40, brothers, sisters and children of someone with Paget's disease may wish to have an alkaline phosphatase

frequently in the spine, skull, pelvis, thighs, and lower legs. In general, symptoms progress slowly, and the disease does not spread to normal bones. Treatment can control Paget's disease and lessen symptoms, but it's not a cure.

What other medical problems can be caused by Paget's disease?

Paget's disease may lead to other medical conditions, including:

- **Arthritis**—Long bones in the leg may bow, distorting alignment and increasing pressure on nearby joints. In addition, Pagetic bone may enlarge, causing joint surfaces to undergo excessive wear and tear. In these cases, pain may be due to a combination of Paget's disease and osteoarthritis.
- **Hearing loss**—Loss of hearing in one or both ears may occur when Paget's disease affects the skull and the bone that surrounds the inner ear. Treating the Paget's disease may slow or stop hearing loss. Hearing aids may also help.
- **Heart disease**—In severe Paget's disease, the heart works harder to pump blood to affected bones. This usually does not result in heart failure except in some people who also have hardening of the arteries.
- **Kidney stones**—Kidney stones are somewhat more common in patients with Paget's disease.
- **Nervous system pressure**—Pagetic bone can cause pressure on the brain, spinal cord, or nerves, and reduced blood flow to the brain and spinal cord.
- **Bone sarcoma**—Paget's disease is associated with the development of osteosarcoma, a malignant tumor of bone. It is, fortunately, rare and occurs in less than 1% of all patients with Paget's disease. However, when there is a sudden onset or worsening of pain, sarcoma should be considered.
- **Teeth loosening**—When Paget's disease affects the facial bones, the teeth may become loose. Disturbance in chewing may also occur.
- **Decreased vision**—Rarely, when the skull is involved, the nerves to the eye may be affected, causing some loss of vision.

What is the relationship between Paget's disease and osteoporosis?

None. Paget's disease is not associated specifically with osteoporosis. Although Paget's disease and osteoporosis can occur in one and the same person, they are completely different disorders. But despite their marked differences, many treatments for Paget's disease can also be used to treat osteoporosis.

What type of medical specialists are generally knowledgeable about

blood test every two or three years. If the alkaline phosphatase level is above normal, other tests such as a bone-specific alkaline phosphatase test, bone scan, or x-ray can be done.

What are the symptoms of Paget's disease?

Many people do not know they have Paget's disease because they have a mild case of the disease with no symptoms. Sometimes, symptoms may be confused with those of arthritis or other disorders. In other cases, the diagnosis is made only after complications have developed. Symptoms can include:

- **Bone pain** is the most common symptom. Bone pain can occur in any bone affected by Paget's disease and is often worse at night. It often localizes to areas adjacent to the joints and can be accompanied by warmth to the touch.
- **Headaches and hearing loss** may occur when Paget's disease affects the skull.
- **Pressure on nerves** may occur when Paget's disease affects the skull or spine.
- **Increased head size, bowing of limb, or curvature of spine** may occur in advanced cases.
- **Hip pain** may occur when Paget's disease affects the pelvis or thighbone.
- **Damage to cartilage of joints** may lead to arthritis.

How is the diagnosis made of Paget's disease?

Paget's disease may be diagnosed using one or more of the following tests:

- **X-rays**—Pagetic bone has a characteristic appearance on x-rays.
- **Alkaline phosphatase test**—An elevated level of alkaline phosphatase in the blood can be suggestive of Paget's disease but can be found in other conditions.
- **Bone scan**—This is useful in determining the extent and activity of the condition. If a bone scan suggests Paget's disease, the affected bone or bones should be x-rayed to confirm the diagnosis.

What is the prognosis (outlook) with Paget's disease?

The outlook is generally good, particularly if treatment is given before major changes in the affected bones have occurred. Paget's disease occurs most

treating Paget's disease?

The following types of medical specialists are, as a rule, generally knowledgeable about treating Paget's disease:

- Endocrinologists—internists who specialize in hormonal and metabolic disorders.
- Rheumatologists—internists who specialize in joint, muscle, and immune disorders.
- Other specialists—Orthopedic surgeons, neurologists, and otolaryngologists (physicians who specialize in ear, nose, and throat disorders) may be called upon to evaluate and treat certain symptoms.

What is the goal of drug treatment?

The goal of treatment is to control Paget's disease activity for as long a period of time as possible. Incidentally detected Paget's disease that is not associated with symptoms may require no treatment. Treatment options include aspirin, other anti-inflammatory medications, pain medications, and medications that slow the rate of bone turnover, such as calcitonin (Calcimar, Miacalcin), etidronate (Didronel), alendronate (Fosamax), and pamidronate (Aredia). A newer drug, risedronate (Actonel), appears to have a powerful effect against severe Paget's disease. It has the added advantage of requiring only two months of initial treatment and is given by mouth.

What medications are approved for Paget's disease?

The U.S. Food and Drug Administration (FDA) has approved the following treatments for Paget's disease:

Bisphosphonates

Five bisphosphonates are currently available for Paget's disease. As a rule, oral bisphosphonate tablets should be taken with 6-8 oz. of tap water on an empty stomach. None of these drugs should be used by people with severe kidney disease. If tolerable, bisphosphonates are the first option of treatment.

- Didronel (etidronate disodium)—tablet; approved regimen is 200-400 mg once daily for six months; the higher dose (400 mg) is more commonly used; no food, beverages, or medications for two hours before and after taking; course should not exceed six months, but repeat courses can be given after rest periods, preferably of three to six months duration
- Aredia (pamidronate disodium)—intravenous (particularly helpful for those patients who cannot tolerate oral bisphosphonates due to gastrointestinal

toxicity); approved regimen 30 mg infusion over four hours on three consecutive days; more commonly used regimen 60 mg over two to four hours for two or more consecutive or nonconsecutive days

- Fosamax (alendronate sodium)—tablet; 40 mg once daily for six months; patients should wait at least 30 minutes after taking before eating any food, drinking anything other than tap water, taking any medication, or lying down (patient may sit)

- Skelid (tiludronate disodium)—tablet; 400 mg (two 200 mg tablets) once daily for three months; may be taken any time of day, as long as there is a period of two hours before and after resuming food, beverages, and medications

- Actonel (risedronate sodium)—tablet; 30 mg once daily for two months; patients should wait at least 30 minutes after taking before eating any food, drinking anything other than tap water, taking any medication, or lying down (patient may sit)

Calcitonin

- Miacalcin is administered by injection; 50 to 100 units daily or three times per week for six to 18 months.

When may surgery be recommended for Paget's disease?

Medical therapy prior to surgery helps to decrease bleeding and other complications. Patients who are having surgery should discuss pretreatment with their physician. There are generally three major complications of Paget's disease for which surgery may be recommended.

- **Fractures**—Surgery may allow fractures to heal in better position.

- **Severe degenerative arthritis**—If disability is severe and medication and physical therapy are no longer helpful, joint replacement of the hips and knees may be considered.

- **Bone deformity**—Cutting and realignment of Pagetic bone (osteotomy) may help painful weight-bearing joints, especially the knees.

Complications resulting from enlargement of the skull or spine may injure the nervous system. However, most neurologic symptoms, even those that are moderately severe, can be treated with medication and do not require neurosurgery.

How do diet and exercise help in Paget's disease?

In general, people with Paget's disease should receive 1,000-1,500 mg of

calcium, adequate sunshine, and at least 400 units of vitamin D daily. This is especially important in patients being treated with bisphosphonates. Patients with a history of kidney stones should discuss calcium and vitamin D intake with their physician.

Exercise is very important in maintaining skeletal health, avoiding weight gain, and maintaining joint mobility. Since undue stress on affected bones should be avoided, patients should discuss any exercise program with their physician before beginning.

Who discovered Paget's disease?

Paget's disease is named after the English surgeon, Sir James Paget, who described it in 1877. Paget also discovered the worm that causes trichinosis and described what is called Paget's disease of the breast. Together with Rudolph Virkow in Germany, Paget was one of the founders of pathology.

Where can I find more information about Paget's disease?

For further information, you can contact:

The Paget's Disease Foundation
120 Wall Street
Suite 1602
New York, NY 10005-4001
212-509-5335
212-509-8492 Fax
email: pagetfdn@aol.com

Paget's Disease At A Glance

- Paget's disease is a chronic bone disorder.
- Paget's disease frequently causes no symptoms.
- Paget's disease can cause pain in the bones or joints, headaches and hearing loss, pressure on nerves, increased head size, bowing of limb, or curvature of spine.
- Tests used to diagnose Paget's disease include x-rays, blood tests, and bone scanning.
- Paget's disease can lead to other medical conditions.
- Treatment options include aspirin, other anti-inflammatory medications, pain medications, and medications that slow the rate of bone turnover.

Reference: Paget's Disease. *New England Journal of Medicine* 2006;355:593-600.

PAGET'S DISEASE AND OSTEOARTHRITIS

Many people who have Paget's disease also develop osteoarthritis. However, this is not the case for all Paget's disease sufferers.

Q. What is osteoarthritis?

A. Osteoarthritis (literally: inflammation of bone and joint) is a condition that can cause a slow progression of joint pain, stiffness, and limitation of movement. Any joint may be involved, but weight-bearing joints such as the hip and knee, as well as the spine (particularly the lumbar spine), are most commonly affected.

Osteoarthritis is caused by changes in the cartilage (a rubbery, shock-absorbing structure in the joint on the ends of the bone), bone, ligaments, and muscle around the joint. When cartilage is no longer smooth and rubbery, movement puts excessive pressure on the bone, often causing pain.

Osteoarthritis may lead to reduced function and, in some cases, can cause severe disability.

Q. What is the relationship between Paget's disease and osteoarthritis?

A. There are several ways that Paget's disease may cause osteoarthritis:

- Paget's disease often alters the normal design of the bone under the cartilage of the joint.
- Paget's disease may cause the long bones (such as the bone of the thigh or leg) to bow (curve) and bend, placing abnormal stresses on the joint.
- Enlargement of the bones in the spine may cause the normal curvature of the back to change.
- The pelvis may become softened, causing the hips to develop osteoarthritis and pushing the pelvis inward. If this happens, the person may have difficulty standing.

Q. When someone has both Paget's disease and osteoarthritis, how is the osteoarthritis diagnosed?

A. The diagnosis of osteoarthritis in Paget's disease usually includes blood tests and an x-ray. The bone changes found on the x-ray are helpful in diagnosing both osteoarthritis and Paget's disease. Blood and urine tests often help rule out other possible causes of arthritis. There is no easy way to distinguish the two conditions, and the judgment of the physician is critically important in making the decision.

Q. How is the osteoarthritis that is associated with Paget's disease treated?

A. The goal of therapy for osteoarthritis is to relieve pain and to improve and preserve joint function. The treatment plan can include medications, physical/occupational therapy, mechanical devices, weight control, exercise, and application of heat or cold to reduce muscle spasm. Treatment may also include an injection with a steroid medication (if inflammation is present), other medications that reduce inflammation, and medications that reduce pain. Under

certain circumstances, surgery may be needed. The prognosis following hip or knee surgery for osteoarthritis is excellent, even in the presence of Paget's disease.

For patients with Paget's disease, pre-operative treatment with anti-pagetic therapy helps to decrease bleeding and other complications during surgery. If you have Paget's disease and are having surgery on the joint affected by Paget's disease, be sure to discuss pre-treatment with your physician.

Q. What is the overall outcome for people who have both Paget's disease and osteoarthritis?

A. Since effective therapies are available for both Paget's disease and osteoarthritis, the combination of Paget's disease and arthritis in the same patient need not be severe.

For arthritis information, call the toll-free Arthritis Foundation Information Line: (800) 283-7800. In Canada, call The Arthritis Society at (416) 979-7228.

For additional information, contact:

The Paget Foundation
120 Wall Street, Suite 1602
New York, NY 10005-4001
Tel (800) 23-Paget or (212) 509-5335
Fax (212) 509-8492
Email: pagetfdn@aol.com
http://www.paget.org

Pain and Paget's Disease

There are several types of pain associated with Paget's disease. Pain is the most common symptom that brings a Paget's disease patient to a physician. Pain varies greatly from patient to patient depending on the location and extent of the Paget's disease and other factors.

Bone Pain

One phase of Paget's disease involves thinning of the bone, which is being aggressively "resorbed" away. This is called "lytic disease." This process can cause small breaks (microfractures) in the bone that are painful, especially when they involve weight-bearing bone. Another source of pain may be from irritation of nerves covering affected bones. Patients usually describe this pain as a deep pain that is most symptomatic at night and may lessen during the day.

Joint and Muscle Pain

When Paget's disease reaches the end of a long bone, the cartilage may degenerate. Also, when pagetic bones are deformed, the adjacent joints are affected. Both of these situations result in osteoarthritis, also referred to as "wear and tear" arthritis, which can be quite painful.

When bones are deformed, the muscles may have to work harder and at abnormal angles, causing muscle pain.

Pain Related to Complications of the Nervous System

A variety of problems, including sciatica (*pain that radiates from the lower back into the legs),* can be related to Paget's disease of the skull and spinal column as a result of pressure on the brain, spinal cord or nerves by enlarged pagetic bones. Pain associated with nervous system complications can affect the head, neck, back and/or extremities.

Treatment for Pain Associated with Paget's Disease

The pain associated with Paget's disease is often alleviated by treating the Paget's disease, treating any accompanying arthritis and also providing non-specific pain relief when needed. Surgery may be necessary when severe pain cannot be controlled by medications.

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Which Paget's Patients Should Be Treated?

The question of which Paget's patients should be treated is a very important and sometimes difficult one for Paget's patients and health professionals.

It has been difficult to generalize about this for two important reasons. First, no two Paget's patients are alike in how they are affected. Second, it is impossible to accurately predict if an asymptomatic patient will develop symptoms or a complication such as a fracture.

Paget's disease experts have suggested that there are three categories of patients who should be treated with the anti-Pagetic drugs, Didronel®, Aredia®, Actonel®, Fosamax®, Skelid®, and Miacalcin®.

The first category of patients, those who have "active disease" include:

- Patients with an elevation of serum alkaline phosphatase (SAP).
- Patients who experience symptoms such as bone pain in a bone affected by Paget's disease.
- Patients who have evidence of an impending fracture.
- Patients who have headache resulting from Paget's disease in the skull, back pain from vertebrae affected by Paget's disease or any other neurological symptoms directly associated with Paget's disease.

The second category of patients includes:

- Patients who require pre-treatment for surgery on bones affected with Paget's disease.
- Patients who develop hypercalcemia, a rare condition which occurs when a patient with several bones affected with Paget's disease and a high SAP is immobilized.

The third category of patients includes:

- Patients who are asymptomatic but who have active Paget's disease in the skull, the long bones or the vertebrae.
- Patients who have Paget's disease in bones next to major joints and, therefore, are at risk for developing arthritis.

The preferred drugs are the three most potent anti-Pagetic drugs, Aredia®, Actonel®, and Fosamax®. Patients who cannot tolerate these bisphosphonate drugs can be treated with injectible Miacalcin®.

For additional information contact:

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SURGERY AND PAGET'S DISEASE

Though surgery is rarely required for Paget's disease, there are several situations when it should be considered.

I. Fractures

The bones affected by Paget's disease are more fragile than other bones, and are more easily fractured and slower to heal. Fractures in Pagetic bone are also less stabile, and treatment requires longer periods of immobility. Such long-term immobilizations can weaken already fragile bones.

A surgical approach to Pagetic fractures does not speed up the healing process but it may help the fracture heal better, and shorten the recovery periods. An orthopedic surgeon should be consulted on which fractures are best managed with non-surgical treatments, and which require surgery.

II. Arthritis

Arthritis is a common complication for many patients with Paget's disease. The reason for this is that Paget's may change the shape of bones, cause bowing and distort the usual alignment of the bones. As a result, the misaligned bones put pressure on the adjacent joints. This can be very painful. Pagetic bones can also become enlarged, causing excessive wear and tear on the joints.

Unlike the pain related to Paget's, arthritis pain responds best to non-steroidal, anti-inflammatory medications, devices that aid mobility, physical therapy and rest. For most people, non-surgical approaches are sufficient, but when the pain is severe and the joints are deformed so that normal function is limited, both an orthopedic surgeon and a rheumatologist should be consulted. The hip joint and the knees are the sites of most of these arthritis-related surgeries.

It is very important that the doctors involved in the surgery, and the pre- and post-surgical treatment, be knowledgeable about Paget's disease and that the general health of the patient be a factor in the pre-surgical decision-making process.

Preparation for a total hip replacement should include a complete medical evaluation (dental, urologic, autologous blood donation, etc.). Anti-Pagetic medications (bisphosphonates or calcitonin) should be used to reduce the impact of Paget's on the surgical site and to minimize bleeding. Antibiotics should also be used both prior to and following the surgery.

The results of total hip replacement are good to excellent 75 to 85% of the time for Paget's patients. The risk for major complications in non-Pagetic bones is 1 to 2%; it is slightly higher in patients with Paget's but research and technological advances may improve these statistics in the future.

III. Progressive Deformity of Lower Limb Weight-Bearing Bones

Paget's may cause deformity in leg bones -- especially bowing of the tibia. When the pain is debilitating and does not respond to medication, an osteotomy (surgical cutting of the bone) may be used to realign the weight-bearing joints, usually the knee but

sometimes the ankle. Osteotomy minimizes stress on the bones and ligaments of these weight-bearing joints, and can alleviate pain and restore normal function. The pre-surgical use of bisphosphonates or calcitonin can help decrease intraoperative bleeding and other complications.

Tibial osteotomy is a major but often effective surgical procedure. Patients with Paget's should consider it only after less invasive treatments have failed to produce positive results.

IV. Neurological Complications of Spinal Paget's Disease

Compression of the spinal cord of the nerves arising from the cord may occur as a result of enlarged vertebra and adjacent bone. Symptoms that may be associated with spinal Paget's disease include back pain, numbness and tingling of the feet, difficulty in walking, paralysis of the legs and abnormal bladder and bowel function.

For patients who remain symptomatic despite medical treatment, surgery may be done to remove the overgrown bone, which is impairing nerve function. The results of this surgery are generally good.

IV. Complications of Paget's Disease Affecting the Skull

Paget's disease in the skull is commonly associated with hearing loss. In some cases, this has been thought to be due to Paget's disease in the small bones in the ear (ossicles), which transmit sound impulses.

In the past, surgery was attempted on these bones to improve hearing, but results of this type of surgery have been generally unsuccessful.

Rarely, the thickness of the skull becomes so great that brain structures may become compressed at the base of the skull. In some cases, fluid may expand the cavities in the brain. This may cause difficulty walking, abnormal bladder function and decreased mental function. A variety of neurosurgical procedures may be required to treat these complications.

Summary

Surgery is rarely necessary in Paget's disease but can offer a welcome opportunity for relief of pain and return of function when other treatment has not been effective.

For additional information contact:

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Email: pagetfdn@aol.com
Website: http://www.paget.org

EXHIBIT 5

Osteomalacia

Read comments received on this topic or add your personal experience

Please note, your computer must have Scripting enabled in order for you to be able to submit patient experience.

DISCLAIMER: Submissions to the Patient Experience section of Patient UK are the views and opinions of the individual contributors. This is an open forum for opinion and comment. Patient UK can take no responsibility for the accuracy or reliability of any medical or other opinions expressed in this section.

1. Created on 15/11/2006

My condition started 2 1/2 years ago when I experienced an inflamation in my feet 6 months after starting to wear custom made orthodic inserts. The reason I saw a Podiatrist was because of being diagnosed with diabetes a year or two earlier. My diabetes is controlled by diet. Am not on any medication for it. My doctor recommended physiotherapy for the inflammation. I had weekly treatments for about two months. These treatments started in January 2004, however, did not help my feet or legs and were incredibly painful. At the same time of the foot inflamation my blood pressure went up so was put on medication for it and is well controlled. In addition was prescribed Lipitor for high cholestrol. (Stopped taking the Lipitor one year ago) Stopped the physio treatments as they didn't help and started exercising under supervision of a therapist. All along I seemed to get worse instead of better. Stopped the exercising and did some aqua sizing over the winter. Had started using a cane in the summer and started using a walker in the latter part of the winter as felt safer walking with it in the snow and ice, also on wet floors at the pool. My pain manifested itself in my thighs, hips, lower back, bottom of my ribs, shoulder blades and upper arms. I couldn't differeniate if my pain was from bone or muscles. It seemed at times to be more from muscles. I have difficulty going up and down steps,sitting down or standing up from a chair, getting in and out of bed and even just shifting around in bed from side to side. Subsequent referral to a rheumatologist and tests and x-rays resulted in a diagnosis of sacroilitis in the fall of 2004. Since that time have seen several specialists who checked my kidneys, bladder and extremities for possible nerve damage. They appear to be allright with the exception of my wrists having carpel tunnel syndrome which I think has resulted from the use of my canes and walker. Had cortizone injections in my SI joints this past summer. Didn't seem to help much. Had a bone density test at the same time when referred to the specialist for the shots. Resulted in doctor saying I had osteoporosis and tests showed severe Vitamin D deficiency. Am taking mega Vitamin D, 5000 units a day plus 1300 mg of calcium, and due to dental problems am not taking the recommended therapy of Actonel for the osteoporosis. Saw my own rheumatologist two weeks ago who has periodically been checking over my file. She has been puzzled all along by blood test results showing elevated alkaline phosphates. Now coupled with the vitamin D deficiency she feels my problems are caused by ostomalacia. The really definitive test would be a bone biopsey, however, will do three months of the mega vitamin D and see how my symptoms fare. I do hope it is this because with osteomalcia at least I have a chance of getting better.

If you find this comment unsuitable or offensive, please click here

EXHIBIT 14

health

Osteomalacia

What is osteomalacia?
Osteomalacia means "soft bones." Osteomalacia is a disease that weakens bones and can cause them to break more easily. In osteomalacia, the bone tends to break down faster than it can re-form.

What causes osteomalacia?
Osteomalacia develops because of a lack of vitamin D (often from not getting enough sunlight) or because of a digestive or kidney disorder. These disorders can interfere with the body's ability to absorb vitamins.

What are the symptoms of osteomalacia?
The most common symptoms of osteomalacia are pain in the bones and hips, bone fractures, and muscle weakness.

How is osteomalacia diagnosed?
There are various tests that can be performed to determine if someone has osteomalacia. Low levels of vitamin D or calcium or a significant drop in phosphate levels may indicate the presence of osteomalacia. X-rays may be taken to see if there is any evidence of osteomalacia development. Also, a bone mineral density scan may be performed to determine if there has been a reduction in bone density. Bone mineral density scans use a special kind of x-ray to measure the amount of calcium and other bone minerals within the body. The higher the mineral content, the stronger the bones; the lower the mineral content, the weaker the bones.

Finally, the doctor may perform a bone biopsy, in which sample bone tissue is taken and examined.

How is osteomalacia treated?
Patients who have osteomalacia can take vitamin D, calcium, or phosphate supplements, depending on the individual case. For instance, people with intestinal malabsorption (the intestines cannot absorb nutrients or vitamins properly) may need to take larger quantities of vitamin D and calcium.

Other treatments to relieve or correct osteomalacia symptoms may include:

- Wearing braces to reduce or prevent bone irregularities
- Surgery to correct bone deformities (in severe cases)
- Adequate exposure to sunlight

Click here to go to the Diabetes and Metabolism, Department of Endocrinology Web site.

EXHIBIT 6

DEPARTMENT OF CORRECTIONS
SAN QUENTIN STATE PRISON

SOAPE NOTE

PATIENT: CARMICHAEL, RAYNELL **CDC:** D25366

DATE OF BIRTH: 04/17/1951 **DATE OF SERVICE:** 09/06/2007

HOUSING UNIT: 2 NORTH 1 LOW **PAROLE DATE:** LIFER

PROBLEM LIST:
1. Hypertension.
2. Hyperlipidemia.
3. Osteoarthritis.
4. Vitamin D deficiency.
5. Persistently elevated alkaline phosphatase.
6. Obesity.

CURRENT MEDICATIONS: Vitamin D 50,000 units p.o. every week, Naprosyn 500 mg p.o. _____ p.r.n., omeprazole 20 mg 1 p.o. every day to be taken with the Naprosyn as needed, hydrochlorothiazide 25 mg 1 p.o. every day, psyllium powder 1 tsp t.i.d., atorvastatin 20 mg 4 p.o. every day, carvedilol 12.5 mg 1 p.o. b.i.d., lisinopril 20 mg 1 p.o. every day, simethicone 80 mg 2 tablets b.i.d. p.r.n., MS Contin 30 mg 2 p.o. q.a.m. 1 p.o. q.p.m., amitriptyline 30 mg p.o. q.h.s.

SUBJECTIVE: Mr. Carmichael presents today for followup. He continues to have complaints of joint aches. He did receive joint injection into his left shoulder, and he has reported that the pain has become much improved. He has also noticed the improvement in the numbness and tingling he was previously having in his hands. He did see the endocrinologist; and while I do not have his report, Mr. Carmichael provides information that the endocrinologist had recommended him starting off on calcium although I did obtain a GI consult to follow back in 60 days for a recheck. Mr. Carmichael reports that he has been having intermittent stomach bloating and increased gas. He had been started on simethicone for his complaints in the past; however, he reports this has not been helping. He is also taking omeprazole, and this is mainly started in the past to use with his NSAIDs. He does not notice any improvement with his medications. He denies any current bowel problems. In the past, he had problems with constipation and underwent a colonoscopy on 8/24/06 that showed a left colon polyp which was an adenoma. Mr. Carmichael today also reports that he does have a history of lactose intolerance and frequently avoids any dairy products.

OBJECTIVE:
VITAL SIGNS: Blood pressure 128/84, pulse rate 76, respiratory rate 20, temperature 98.4, weight 295 pounds.
GENERAL: Awake, alert oriented gentleman in no acute distress.
LUNGS: Clear to auscultation.
HEART: Regular rate and rhythm. No gallops, rubs, or murmurs.
ABDOMEN: Soft, obese, nondistended, and nontender.

CDC: [illegible]366

EXTREMITIES: No cyanosis, clubbing, or edema. Evaluation shows some crepitus in the bilateral knees. No effusion. Hand exam shows no effusion. No synovitis. No soft tissue swelling. No increased warmth and no erythema. Similarly, his wrists, elbows, and shoulders show no inflammation, synovitis, or effusion.

Labs drawn on 7/25/07; sodium 139, potassium 4.3, chloride 101, bicarb 20, BUN 14, creatinine 1.2, glucose 93, calcium 98, albumin 4.3, total protein 7.6. AST 20, ALT 25, alkaline phosphatase 305. Alkaline phosphate isoenzymes show intestinal enzyme of 15, bone isoenzyme of 224, and total alkaline phosphatase isoenzyme of 292. Vitamin D 125 total with 64, TSH 1.18.

ASSESSMENT:

1. Hypertension well controlled.
2. Hyperlipidemia stable on atorvastatin.
3. Vitamin D deficiency. The patient has been on vitamin D supplementation. After he left, we were able to obtain the report from the endocrinologist. He was seen by Dr. O'Connor on 8/24/07. He recommended to start ergocalciferol 500 IU every week, oral calcium 1,000-1,500 mg orally per day, and followup in 2 months with labs prior to appointment to include vitamin D 125, hydroxy levels, comprehensive metabolic panel, and an intact PTH. She also recommended GI consult to evaluate to see if there was any component of GI malabsorption contributing to the patient's deficiency and also rheumatology consult.
4. Persistently-elevated alkaline phosphatase. The patient has had a replacement with vitamin D. We did a fairly comprehensive review of his medical records today. In the past, he did have a bone scan which had areas of increased uptake including the proximal femurs bilaterally, and the right clavicle. Bilateral head films done on 3/2/07 showed surface white thickening in the proximal femurs bilaterally which they thought was developmental. He had an x-ray of his left shoulder which showed a narrowing of the inferior portion of the AC joint. Left shoulder girdle was unremarkable. He has not had any imaging studies of the right shoulder as his complaints in the past, while bilateral, where more involved with the left shoulder. Exact etiology of his elevated alkaline phosphatase may, in fact, be multifactorial. He certainly has osteoarthritis. He also has vitamin D deficiency. Failure of his alkaline phosphatase to improve with replacement may indicate other process, and I think we need to consider Paget disease in our differential diagnosis.
5. Osteoarthritis. The patient has had improvement in his left shoulder pain after injections. We will continue to monitor.
6. Gastrointestinal complaints, fairly nonspecific complaints of bloating and gas may in fact due to component of lactose intolerance. We also may consider other causes which could lead to a malabsorption of vitamin D, specifically celiac sprue, although might be less likely in this patient.

PLAN:

1. We will continue his medications.
2. We will add calcium 500 mg p.o. t.i.d.
3. We will refer to GI for evaluation.
4. We will order lab tests to include a urine hydroxyproline to evaluate for Padget.
5. We will check an IgA and endomysial antibody and IgA antitransglutaminase antibody to evaluate for sprue.
6. In the past, he had a UCSF consult, and they had recommended a repeat SPAP and UPAP to evaluate for MGUS in 1 year, and we will go ahead and repeat that at this time.

CDC: D23366

7. We will also check a right clavicular series and shoulder series to evaluate for Paget disease. If the plain films do show findings consistent with Paget, we will consider starting him on ~~alendronate~~ Fosamax 40 mg p.o. every day to see if this will help with his complaints of pain and also his elevated alkaline phosphatase.
8. He is to return to clinic in 3 weeks for a followup, sooner if he has any problems.

CLARENE DAVID, M.D.

CD/sts
D: 09/06/2007 21:31:00
T: 09/07/2007 22:33:44
Job #: 36080

Report View

Patient Demographics Done Print

Requisition Number: **193618**
Patient Name: **CARMICHAEL,RAYNELL**
Age: **56**
Birth Date: **04/17/1951**
Gender: **M**
Social Security Number:
Accession Number: **GQ9204852**
Urine Volume:
Lab Ref Num: **2N1**
Report Comments:

Client: **4810945**
Referring Physician: **RAND**
Room/Loc:
Patient Id: **D25366**
Patient Phone:
Collected: **10/15/2007 10:25AM**
Logged: **10/15/2007 01:00AM**
Reported: **10/16/2007 08:11AM**

Report Name	Results	Units	Reference Range	Site
COMPREHENSIVE METABOLIC PANEL				SC
SODIUM, SERUM:	136	mmol/L	135-146	
POTASSIUM, SERUM:	5.2	mmol/L	3.5-5.3	
CHLORIDE, SERUM:	100	mmol/L	98-110	
CARBON DIOXIDE (CO2):	20	mmol/L	16-26	
UREA NITROGEN,BLOOD (BUN):	34 (H)	mg/dL	7-25	
CREATININE, SERUM:	1.8 (H)	mg/dL	0.5-1.3	
GLUCOSE:	82	mg/dL	65-99	
CALCIUM, SERUM:	10.4 (H)	mg/dL	8.6-10.2	
TOTAL PROTEIN:	7.7	g/dL	6.2-8.3	
ALBUMIN:	4.1	g/dL	3.6-5.1	
GLOBULIN, TOTAL:	3.6	g/dL	2.1-3.7	
A/G RATIO:	1.1	ratio	1.0-2.1	
AST (SGOT):	15	U/L	10-35	
BILIRUBIN, TOTAL:	0.4	mg/dL	0.2-1.2	
ALT (SGPT):	25	U/L	9-60	
ALKALINE PHOSPHATASE:	297 (H)	U/L	40-115	
eGFR:	42 (L)		SEE BELOW	
	REFERENCE RANGE: > = 60 ml/min/1.73m2 IF PATIENT IS AFRICAN AMERICAN, MULTIPLY REPORTED RESULT BY 1.21.			
CREATINE KINASE (CK)				SC

EXHIBIT 3

Copy

SAN QUENTIN STATE PRISON
HEALTH CARE SERVICES/NOTES

PATIENT: CARMICHAEL,RAYNELL CDCR# D-25366
DATE OF BIRTH: April 17, 1951 DATE OF SERVICE: 12-21-07
HOUSING UNIT: 2-N-1-L
Physician (MD) Dr. RAND, MD

High Risk/Chronic Care/Problems/Symptoms.

I am concern about my "CHOLESTEROL" Due to the Fact that I haven't had any medication to treat this problem every since I left the Hospital Oct 13, 2007, I am requesting that I be consider other medicie like VyTORIN-Zetia,etc. Crestor

I am still having problem with my left leg-Toe-Foot/hand etc. These symptoms was stated as far back as August 9, 2007, That I still feel tired a sick feeling and feverish that has manifested with in my whole body.Lower back, left leg, foot/toe, Left shoulder blade elbow, Neck,The same holds true to my right side of my body. it's hardto differeniate if the pain, numbness, stiffness, nerves are from my bones or muscles it still is hard and difficult sitting down or standing up from a chair, getting in and out of bed, even shifting around in bed from side to side etc. I would like to know the results from the MRI-C.T. Bone Scan.

X I am requesting a wedge pollow to see if it would be helpfull in sleeping!?

RC I am requesting to be seen by an"ORTHOPEDIO" Doctor and"RHEUNATOLOGIST" Due to the Fact that my right knee has pain numbness, stiffness, poping and cracking plus grinding bone to bone. also my left shoulder & Elow.

OUESTION??? After you review of the MRI & CT-Bone Scan are the PITTED SPOTS and MOTTLED LESION -Permanet Damage??? Yes or No , and what do you think causes it

Question How am I being treated for Anema ? is my B-12-count Low. I would like an answer to this.

Problem, My hands and Body are sllowen, what is the cause of this???

Medication Refill =LISNOPRIL 5mgs STOP-12-14-2007
AMITRIPTYLINE 30mgs STOP-12-14-2007

I am requesting to be seen by an dietician, to put together an 1500-2000 Calories a day using San Quentin weekly Menu.

Cc:

EXHIBIT B

STATE OF CALIFORNIA
CDC 7362 (Rev. 03/04)

HEALTH CARE SERVICES REQUEST FORM

865120

DEPARTMENT OF CORRECTIONS

PART I: TO BE COMPLETED BY THE PATIENT

A fee of $5.00 may be charged to your trust account for each health care visit.

If you believe this is an urgent/emergent health care need, contact the correctional officer on duty.

REQUEST FOR: MEDICAL ☒ MENTAL HEALTH ☐ DENTAL ☐ MEDICATION REFILL ☒

NAME	CDC NUMBER	HOUSING
Carmichael, Raynell	D-25366	2Nl-L

PATIENT SIGNATURE

DATE: Jan 7, 2008

REASON YOU ARE REQUESTING HEALTH CARE SERVICES. (Describe Your Health Problem And How Long You Have Had The Problem) METHOCARBAMOL 750 mgs, 2 x 1-Tab a day, STOP--1-13-2008

"See Attach" Health Care Services-Notes!!!

NOTE: IF THE PATIENT IS UNABLE TO COMPLETE THE FORM, A HEALTH CARE STAFF MEMBER SHALL COMPLETE THE FORM ON BEHALF OF THE PATIENT AND DATE AND SIGN THE FORM

PART III: TO BE COMPLETED AFTER PATIENT'S APPOINTMENT

☐ Visit is not exempt from $5.00 copayment. (Send pink copy to Inmate Trust Office.)

PART II: TO BE COMPLETED BY THE TRIAGE REGISTERED NURSE

Date / Time Received:	Received by:
Date / Time Reviewed by RN:	Reviewed by:

S: Pain Scale: 1 2 3 4 5 6 7 8 9 10

O: T: P: R: BP: WEIGHT:

A:

P:

☐ See Nursing Encounter Form

E:

APPOINTMENT SCHEDULED AS:	EMERGENCY (IMMEDIATELY) ☐	URGENT (WITHIN 24 HOURS) ☐	ROUTINE (WITHIN 14 CALENDAR DAYS) ☐

REFERRED TO PCP:	DATE OF APPOINTMENT:
COMPLETED BY	NAME OF INSTITUTION

PRINT / STAMP NAME	SIGNATURE / TITLE	DATE / TIME COMPLETED

CDC 7362 (Rev. 03/04) Original - Unit Health Record Yellow - Inmate (if copayment applicable) Pink - Inmate Trust Office (if copayment applicable) Gold - Inmate

EXHIBIT 16

SAN QUENTIN STATE PRISON

HEALTH CARE SERVICES/NOTES

PATIENT: CARMICHAEL,RAYNELL CDCR# D-25366

DATE OF BIRTH: April 17, 1951 DATE OF SERVICE: Jan 7, 2008

HOUSING UNIT: 2-N-1-L

Physician (MD)

High Risk/Chronic Care/Problems/Symptoms. CDC No. 835120

Problems: My hands, and Body are still swollen, It hurts when clenching and unclenching my hands. This has been happening every sence I was discharge from Marin General Hospital On Oct 13, 2007, I've been complaing to Dr. RAND at each visit. I am still not receiving any type of treatment ?

I want to know ? ? am I still a Anemic

Dr. RAND you didn't answer my question about the Radiology report, that the Bone disease handn't spreaded any more from 7-6-2006,-12-14-2007, so does it mean that the Damage done is PERMANET!? I would like to see the Picture of the CT-Bone Scan. I would like a answer to this these question, If you are not able , Please tell me who can!?

I am still requesting that I be seen by an RHEUNATOLOGIST & Gastrointestinal as recommended by Dr. O'Conner on 8-24-2007, He believes the GI Malabsorption could be contributing to the patient's Vitamin D deficiency & Bone disease.

I still haven't been treated to control my CHOLESTEROL Leaves, with Medication it needs to be check & I be consider for Zetia, Vytorin

My right and Left Knees hurt when walking and sitting along time when I get up I've pain stiffness, numbness. I need some type of Osteoarthritis Medication.

I am still experiencing constant numbness and tingling in my 3rd & 4th fingers and Tumb on both hands.

When walking long distances a sharp pain in my lower back radiates down my left leg & foot.

I want to know when am I going to be schedule to be seen by Dr. Schobock a Bone and Matabolism specialist.

This is to be place with in my medical files.

Cc:

Copy

EXHIBIT 46

SAN QUENTIN STATE PRISON

HEALTH CARE SERVICES/NOTES

PATIENT: CARMICHAEL,RAYNELL CDCR# D-25366

DATE OF BIRTH: April 17, 1951 DATE OF SERVICE: Feb 27,08

HOUSING UNIT: 2-N-1-L

Physician (MD) Dr. RAND

High Risk/Chronic Care/Problems/Symptoms. #9929155-Feb 19,2008

The last time I seen you was on Jan 18,08, for the refill of METHOCARBAMOL 750 mg 2xa day for Muscles Spasms, you told me that the CMO-Dr. Kannan said that Doctors are to no longer write any more prescription for the medication. You told me the only other choice I have is to is increase my Ms Cotin. that is for pain. I need some thing for my Muscle Spasms. Every since Jan 18,08 My muscle spasms has increase to all over my body. the Methocarbamol STOPs and Controls the Muscle spasm. The Ms Contin that I am taking now hasn't stoped the spasm. I am requesting a substitute Medication for Muscle Spasm.

I am still having Neck problems, Stiffness & Pain, also swelling in my hands pain, numbness in my 3rd & 4th fingers & Thumb.

I am still having stiffness poping, cracking in my right knee grinding bone to bone, this has been an on going problem even more so when not taking NAPROXEN, which I've been off since I return from the Hospital Oct 13, 2007 It's getting Worse, I am not able to lift my right Leg up to far, it husts with pain, this has happen in the past and I was started back on NAPROXEN I was able to lift my right leg better.

I am requesting a wedge Pollow to HELP releave the pain stiffness in NECK AND THE Numbness to fingers in my right and left hand

I am requesting another Back support Brace or Corsets

I am still waiting to be seen by an RHEUNATOLOGIST this request was made in May 2007,

I would like to know my statistic as an Anema and my B12-count which has has been Low in the past.

I would like to know how you are going to Treat me for my CHOLESTEROL Will it be -Zetia-Vytorin or ??? Crestor

The dietician said the Doctor has to Request A 1500 Calories Intake A day

Cc: This is to be place within my Medical files

EXHIBIT 12

SAN QUENTIN STATE PRISON

HEALTH CARE SERVICES/NOTES

PATIENT: CARMICHAEL,RAYNELL CDCR# D-25366

DATE OF BIRTH: April 17, 1951 DATE OF SERVICE: Mar, 27,08

HOUSING UNIT: 2-N-1-L

Physician (MD) Dr. RAND

High Rish/Chronic Care/Problems/Symptoms.

I am still having Constipation, the stool softers are not working ! I need some thing else! I've been getting Milk of MAGNESRA, FROM North Block Clinic

I have been complaing about my right knee every since I return from the Hospital Oct 13,2007 You STOP the NAPROXEN 500 mgs 2xaday, and the METHOCARBAMOL 750mgs 2xaday. Now due to my continuous right knee swelling pain, stiffness, poping & cracking plus grinding bone to bone, as well as all other joints elbow, left shoulder, neck, & hands. I am requesting that my superimposed Osteoarthritis be treated with celebrex 100-200 mgs, I am not able to lift my right leg up to far, it hurts, with pain, this has happen in the past and I was started back on NAPROXEN, I was able to lift my right leg again.

I am still waiting to be seen by an Rheunatologist this request was first made in May 2007, why haven't been seen.?

I would like to now when am I going to be seen by Dr. Papps for spinal treatment.

I still have an Vitamin D-deficiency that still needs to find out the real cause of the problem

I still haven't been seen by the Podiaty. I am ready to have out patient surgery on my toe.

I seen the Dietician in the past she told me in order to recieve an 1500-2000 calories print out of san Quentin MENU you would have to write it in your request, and then she would do it. The dietician name is Ms. Cora PEREA-Ph-Ext# 5977

Cc: This is to be place with in my Medical file

EXHIBIT B

SAN QUENTIN STATE PRISON

HEALTH CARE SERVICES/NOTES

PATIENT: CARMICHAEL, RAYNELL CDCR# D-25366

DATE OF BIRTH: April 17, 1951 DATE OF SERVICE: 4-30-08

HOUSING UNIT: 2-N-1-L

Physician (MD) Dr. V. RAND

High Rish/Chronic Care/Problems/Symptoms.

This issuse was not address on March 27,08, I am not able to lift my Left Leg up! I have been complaing about my right knee every since I return from the Hospital Oct 13, 2007, You STOP the NAPROXEN 500mgs 2xaday, and the METHOCRBAOL 750mgs 2xaday. now due to my continuous right knee swelling pain, stiffness, poping & cracking plus grinding bone to bone, as well as all other joints elbow, left shoulder, neck, & hands, I am requesting that my superimposed Osteoarthritis be treated with Celebrex 100-200 mgs, I am not able to fift my right leg up to far, it hurts with pain, this has happen in the past and I was started back on NAPROXEN, I was able to fift my right leg up again.

This is another issuse that wasn't address on March 27, 08, I am still waiting to be seen by an "Rheunatologist" this request was first made in May 2007, whats the reason why! I haven't been seen!? Did Not Receive water pills IN March!

Request A-ADA-Shower-Chrono

I made this request again about what the dietician said to tell you , now I order to receive an 1500-2000 Calories print out of San Quentin MENU all you have to do is write in your request to the Dietician or Call her Ms. Cora PEREA, Ph-Ext. # 5977,

I still have a Vitamin D-deficiency that still needs to find out the real cause of the problem. Request for Leg Stocking

I still am having Constipation , I am taking fiber, stool softers, I am having lots of gas

I am still experiencing chronic Neck stiffness, pain, pinch nerve C-6&7, numbness, tingling radiating sown my left & Right arm in to my 3rd & 4th fingers and Tumb on both hands, it's worsening!!, I First told you about way back in Dec 21, 07, and I've continued to repeat it I need treatment.

I am still waiting for an "Gastrorintestinal" follow up. I would like to know is it still necessary for me to be seen by Dr. Schobock, a Bone Matabolism Specialist at UCSF!

I am concern about the CHOLESTEROL-Medication-Zetia-it has been in the News! is it Safe

Cc: This is to be place with in my Medical file

EXHIBIT 14

health

Osteomalacia

What is osteomalacia?
Osteomalacia means "soft bones." Osteomalacia is a disease that weakens bones and can cause them to break more easily. In osteomalacia, the bone tends to break down faster than it can re-form.

What causes osteomalacia?
Osteomalacia develops because of a lack of vitamin D (often from not getting enough sunlight) or because of a digestive or kidney disorder. These disorders can interfere with the body's ability to absorb vitamins.

What are the symptoms of osteomalacia?
The most common symptoms of osteomalacia are pain in the bones and hips, bone fractures, and muscle weakness.

How is osteomalacia diagnosed?
There are various tests that can be performed to determine if someone has osteomalacia. Low levels of vitamin D or calcium or a significant drop in phosphate levels may indicate the presence of osteomalacia. X-rays may be taken to see if there is any evidence of osteomalacia development. Also, a bone mineral density scan may be performed to determine if there has been a reduction in bone density. Bone mineral density scans use a special kind of x-ray to measure the amount of calcium and other bone minerals within the body. The higher the mineral content, the stronger the bones; the lower the mineral content, the weaker the bones.

Finally, the doctor may perform a bone biopsy, in which sample bone tissue is taken and examined.

How is osteomalacia treated?
Patients who have osteomalacia can take vitamin D, calcium, or phosphate supplements, depending on the individual case. For instance, people with intestinal malabsorption (the intestines cannot absorb nutrients or vitamins properly) may need to take larger quantities of vitamin D and calcium.

Other treatments to relieve or correct osteomalacia symptoms may include:

- Wearing braces to reduce or prevent bone irregularities
- Surgery to correct bone deformities (in severe cases)
- Adequate exposure to sunlight

Click here to go to the Diabetes and Metabolism, Department of Endocrinology Web site.